WHAT IS CLAIMED IS:

1. A method of detecting a target nucleic acid in a sample, comprising:

a) contacting the sample with at least one AP site probe and an AP endonuclease, under conditions sufficient to allow the AP site probe to hybridize to the target nucleic acid and form a reaction mixture, wherein said AP site probe comprises an oligonucleotide **NA** that hybridizes to the target nucleic acid and a functional tail **R** comprising a detectable reporter group, said functional tail **R** attached via a phosphodiester bond of a phosphate group to the 3′ terminal nucleotide of the **NA**, wherein the reporter group is not detected when the functional tail **R** is attached to the **NA**; and

b) incubating the reaction mixture under reaction conditions sufficient to allow said AP endonuclease to cleave the phosphodiester bond attaching the functional tail **R** to the 3′ terminal nucleotide of the **NA**, wherein the AP endonuclease preferentially cleaves the phosphodiester bond attaching the tail **R** to the **NA** when the **NA** is hybridized with a complementary target nucleic acid sequence in comparison to when the **NA** is unhybridized or hybridized to a non-complementary nucleic acid; and

c) detecting the reporter group on the cleaved functional tail **R**, whereby the target nucleic acid is detected.

2. The method of Claim **1**, further comprising contacting the sample with an enhancer oligonucleotide, wherein the 5′-end of said enhancer oligonucleotide hybridizes to the target nucleic acid on the 3′ side of the hybridized AP site probe, wherein a gap of 0-5unpaired bases resides between the enhancer oligonucleotide and the AP site probe hybridization locations with the target nucleic acid.

3. The method of Claim **2**, wherein the 5'-end of said AP site probe is covalently linked to the 3'-end of said enhancer.

4. The method of Claim **1**, further comprising a quencher molecule attached to the 5′ end of the **NA** of said AP site probe via a non-cleavable linker.

5. The method of Claim **1**, wherein the cleavage of the phosphodiester bond results in a hybridized **NA** having a free 3′-OH.

6. The method of Claim **5**, further comprising contacting the sample with a nucleic acid polymerase, and further comprising amplifying the target nucleic acid, said

amplifying comprising incubating the sample under reaction conditions sufficient to allow the polymerase to extend the hybridized **NA** in a template-specific manner.

7. The method of Claim **6**, wherein said amplifying is isothermal amplification.

8. The method of Claim **5**, wherein the sample is incubated under reaction conditions that simultaneously allow the AP endonuclease to cleave the phosphodiester bond of the AP site probe and the polymerase to extend the cleaved AP site probe in a template-specific manner.

9. The method of Claim **1**, wherein the **NA** of said AP site probe is 3-200 nucleotides in length.

10. The method of Claim **1**, wherein the functional tail **R** is attached to the phosphate group through a hydroxyprolinol linker.

11. The method of Claim **1**, wherein the reporter group is a fluorophore.

12. The method of Claim **1**, wherein the AP endonuclease is a Class II AP endonuclease.

13. The method of Claim **12**, wherein the Class II AP endonuclease is an *E.coli* Endonuclease IV.

14. The method of Claim **1**, wherein the target nucleic acid is attached to a solid support.

15. The method of Claim **1**, wherein the AP site probe is attached to a solid support.

16. The method of Claim **2**, wherein the enhancer is attached to a solid support.

17. The method of Claim **1**, wherein said at least one AP site probe comprises a first AP site probe and a second AP site probe, wherein said first probe comprises a **NA** portion comprising at least one base difference from the **NA** portion of said

second probe, and wherein said first probe comprises a reporter group that is distinguishably detectable from the reporter group of said second probe.

18. The method of Claim **17**, wherein the reporter group of said first probe and said second probe comprises a fluorophore, and wherein the fluorophore of said first probe comprises a distinguishably detectable emission wavelength from the fluorophore of said second probe.

19. The method of Claim **17**, wherein said at least one base difference between the **NA** of said first probe and the **NA** of said second probe comprises a base difference at position 1, 2, 3 or 4 from the 3' end of said probes.

20. The method of Claim **17**, wherein said at least one base difference between the **NA** of said first probe and the **NA** of said second probe comprises a base difference at position 1 or 2 from the 3' end of said probes.

21. The method of Claim **1**, wherein said at least one AP site probe comprises a plurality of AP site probes, wherein the **NA** portion of said probes are members of a universal library.

22. The method of Claim **21**, wherein the **NA** portion of said AP site probe members is 5-8 nucleotides in length.

23. The method of Claim **9**, wherein said AP site probe members further comprise at least one modified base.

24. A kit comprising an AP site probe for carrying out the method of Claim **1**.

25. A method of detecting a target nucleic acid in a sample, comprising:

a) contacting the sample with at least one AP site probe and an AP endonuclease, under conditions sufficient to allow the AP site probe to hybridize to the target nucleic acid and form a reaction mixture, wherein said AP site probe comprises an oligonucleotide **NA** that hybridizes to the target nucleic acid, a functional tail **R** comprising a quencher molecule, said functional tail **R** attached via a phosphodiester bond of a phosphate group to the 3′ terminal nucleotide of the **NA**, and a reporter group attached

via a non-cleavable linker to the 5′ terminal nucleotide of the **NA**, wherein the reporter group is not detected when the functional tail **R** is attached to the **NA**; and

b) incubating the reaction mixture under reaction conditions sufficient to allow said AP endonuclease to cleave the phosphodiester bond attaching the functional tail **R** to the 3′ terminal nucleotide of the **NA**, wherein the AP endonuclease preferentially cleaves the phosphodiester bond attaching the tail **R** to the **NA** when the **NA** is hybridized with a complementary target nucleic acid sequence in comparison to when the **NA** is unhybridized or hybridized to a non-complementary nucleic acid; and

c) detecting the reporter group upon cleavage of the functional tail **R**, whereby the target nucleic acid is detected.

26. A method of amplifying a target nucleic acid sequence in a sample comprising:

a) contacting the sample with at least one forward primer and at least one reverse primer, an AP endonuclease, and a nucleic acid polymerase, under conditions sufficient to allow the forward and reverse primers to hybridize to the target nucleic acid and form a reaction mixture, wherein the forward and the reverse primer independently comprise a sequence structure $(\mathbf{NA_1}\text{-}\mathbf{L})_\mathbf{m}\text{-}\mathbf{NA_2}$, wherein $\mathbf{NA_1}$ and $\mathbf{NA_2}$ are nucleic acid sequences complementary to the target nucleic acid, **L** is an AP endonuclease-cleavable linker, and **m** is from 0 to 100, wherein at least one of said forward and reverse primer comprises an AP endonuclease-cleavable linker, **L**;

b) incubating the reaction mixture under reaction conditions that simultaneously allow the AP endonuclease to cleave at a linker site **L**, thereby generating a free 3′-OH, and the polymerase to extend the primers in a template-specific manner; whereby the target nucleic acid sequence is amplified.

27. The method of Claim **26**, wherein said amplifying is isothermal amplification.

28. The method of Claim **26**, wherein said AP endonuclease is an Endonuclease IV.

29. The method of Claim **1**, wherein said target nucleic acid is a product of an amplification reaction.

1 **30.** The method of Claim **29**, wherein said amplification reaction is
2 polymerase chain reaction.

1 **31.** The method of Claim **29**, wherein said amplification reaction is
2 polymerase chain reaction and said method uses a thermostable endonuclease.

1 **32.** The method of Claim **29**, wherein said amplification reaction is an
2 isothermal amplification reaction.
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